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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/801,982

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Marianna Goldrick

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EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1634

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/12/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/801,982

Applicant(s)

GOLDRICK, MARIANNA

Examiner

Frank W. Lu

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1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

Supplemental Action

1. Based on reviewing the office action mailed on January 4, 2007, the examiner notes that the rejection under 35 U.S.C 103 related to claims 15-18, 23, and 28 is incomplete and PTO-892 has not been scanned into eDAN. Now the examiner issues a supplemental action to address these issues. This supplemental action is used to replace previous action mailed on January 4, 2007.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-4, 7, 8, 10, 11, 14, and 29 are rejected under 35 U.S.C. 102 (a) or (e) as being anticipated by Garvin (US 2003/0170669, published on September 11, 2003 and priority date: April 11, 2000).

Regarding claims 1-3, Garvin teaches a method of obtaining a leukocyte lysate comprising RNA comprising fractionating leukocytes from whole blood using a leukocyte depletion matrix (ie., the filter media) and lysing the fractionated leukocytes to

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obtain a lysate comprising RNA as recited in claim 1 wherein the leukocytes are comprised on the matrix at the time they are lysed as recited in claim 2 (see abstract, page 1, [0006], [0009] and [0018]) and the leukocyte comprising matrix is stored for a period of time (ie., the time between step (a) and step (c) in the method of Garvin) prior to lysis of the leukocytes as recited in claim 3 (ie., page 1, [0009]).

Regarding claims 4, 7, and 8, Garvin teaches that the fractionated leukocytes are contacted with a lysis solution (ie., the solution comprising a chaotropic agent) as recited in claim 4 wherein the lysis solution contains a chaotropic agent and the chaotropic agent is a guanidinium salt (see page 1, [0018]).

Regarding claims 10, 11, and 14, since it is known that guanidinium hydrochloride is a ribonuclease inhibitor, Garvin teaches that the lysis solution comprises a ribonuclease inhibitor (ie., guanidinium hydrochloride) as recited in claim 10, further comprising extracting the RNA from the lysate as recited in claim 11 and further comprising extracting RNA and DNA from the lysate as recited in claim 14 (see page 1, [0018]).

Regarding claim 29, Garvin teaches fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix (ie., the filter media), lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate (see abstract, page 1, [0006], [0009] and [0018]).

Therefore, Garvin teaches all limitations recited in claims 1-4, 7, 8, 10, 11, 14, and 29.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin as applied to claims 1-4, 7, 8, 10, 11, 14, and 29 above, and further in view of Rutter *et al.*, (US Patent No. 4,652,525, published on March 24, 1987).

The teachings of Garvin have been summarized previously, *supra*.

Garvin does not disclose that the guanidinium salt is guanidinium thiocyanate as recited in claim 9.

Rutter *et al.*, teach to isolate mRNA using guanidinium thiocyanate (see column 10, last paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 9 wherein the guanidinium salt is guanidinium thiocyanate in view of the prior art of Garvin and Rutter *et al.*. One having ordinary skill in the art would have been motivated to do so because, comparing with guanidinium hydrochloride, guanidinium thiocyanate is a more effective denaturing agent to inhibit RNase (see column 10, last paragraph). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 9 using

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guanidinium thiocyanate in order to more effectively inhibit RNase during the process for isolating RNA.

6. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Rutter *et al.*, as applied to claims 1-4, 7, 8-11, 14, and 29 above, and further in view of Ala-Kokko *et al.*, (US Patent No. 5,045,449, published on September 3, 1991).

The teachings of Garvin and Rutter *et al.*, have been summarized previously, *supra*.

Garvin and Rutter *et al.*, do not disclose that the lysis solution comprises a detergent wherein the detergent is Triton X-100, Tween-20, SDS (sodium dodecyl sulfate), sarcosyl, or deoxycholic acid as recited in claims 5 and 6.

Ala-Kokko *et al.*, teach to isolate total RNA using a lysis solution comprising sarcosyl and guanidinium thiocyanate (see column 5, third paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 5 and 6 wherein the lysis solution further comprises a detergent such as sarcosyl in view of the prior art of Garvin, Rutter *et al.*, and Ala-Kokko *et al.*. One having ordinary skill in the art would have been motivated to do so because addition of sarcosyl into a lysis solution comprising guanidinium thiocyanate would enhance to lyse the cells during the process for isolating RNA (see column 5, third paragraph). One having ordinary skill in the art at the time the invention was made would have been a reasonable

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expectation of success to perform the method recited in claims 5 and 6 by adding sarcosyl into a lysis solution comprising guanidinium thiocyanate.

7. Claims 12, 13 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin as applied to claims 1-4, 7, 8, 10, 11, 14, and 29 above, and further in view of Maniatis *et al.*, (Molecular Cloning: A Laboratory Manual, pages 191-193, 1982).

The teachings of Garvin have been summarized previously, *supra*.

Garvin does not disclose that extracting the RNA is performed via an organic extraction as recited in claim 12 wherein the organic extraction is a phenol/chloroform extraction as recited in claim 13, and extracting the lysate with an organic solution to form organic and aqueous phases and separating the organic and aqueous phases as recited in claim 26. However, Garvin does teach fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, lysing the fractionated leukocytes to produce a lysate and isolating RNA as recited in claim 26 (see abstract, page 1, [0006], [0009] and [0018]).

Maniatis *et al.*, teach to extract RNA via phenol/chloroform (see page 192).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 12, 13, and 26 by extracting the RNA via phenol/chloroform in view of the prior art of Garvin and Maniatis *et al.*. One having ordinary skill in the art would have been motivated to do so because Garvin suggests to isolate RNA using a known manner (see page 1, [0017] and the RNA isolation method taught by Maniatis *et al.*, is well known method for isolating RNA. One having ordinary skill in the art at the time the invention

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was made would have been a reasonable expectation of success to perform the methods recited in claims 12, 13, and 26 using the RNA isolation method taught by Maniatis *et al.*.

8. Claims 15-18, 23, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin as applied to claims 1-4, 7, 8, 10, 11, 14, and 29 above, and further in view of Korfhage *et al.*, (US Patent No. 6,872,818 B2, priority date: January 25, 2001).

The teachings of Garvin have been summarized previously, *supra*.

Garvin does not disclose prior to lysis, treating the fractionated eukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition as recited in claims 15 and 28 wherein the salt is a sulfate salt as recited in claim 16, the salt is ammonium sulfate as recited in claim 17, the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18, and the matrix is contacted with the RNA preservation composition as recited in claim 23. However, Garvin does teach fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, lysing the fractionated leukocytes to produce a lysate, and isolating RNA from the lysate as recited in claims 23 and 28 (see abstract, page 1, [0006], [0009] and [0018]).

Regarding claims 15-17 and 28, since Korfhage *et al.*, teach to use ammonium sulfate to mitigate or neutralize inhibitory effects of certain molecules that interfere with RNA function or to reduce the detrimental effects of some agents on RNA activity (see abstract and column 2, lines 1-10), Korfhage *et al.*, disclose an RNA preservation

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composition (ie., ammonium sulfate) comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition as recited in claims 15 and 28 wherein the salt is a sulfate salt as recited in claim 16 and the salt is ammonium sulfate as recited in claim 17.

Regarding claim 18, Korfhage *et al.*, teach that the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration (below 20 g/100 ml (see column 1, lines 56-60).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 15-17 by treating the fractionated eukocytes with an RNA preservation composition comprising ammonium sulfate prior to lysis and contacting the RNA preservation with the matrix in view of the prior art of Garvin and Korfhage *et al.*. One having ordinary skill in the art would have been motivated to do so because the Korfhage *et al.*, teach to use ammonium sulfate to mitigate or neutralize inhibitory effects of certain molecules that interfere with RNA function or to reduce the detrimental effects of some agents on RNA activity (see abstract and column 2, lines 1-10) so that the half-life of the RNA is increased. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the methods recited in claims 15-17 by treating the fractionated eukocytes with an RNA preservation composition comprising ammonium sulfate prior to lysis and contacting the RNA preservation with the matrix in order to increase the half-life of the RNA.

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9. Claims 15-23 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin as applied to claims 1-4, 7, 8, 10, 11, 14, and 29 above, and further in view of Lader (US Patent No. 6,204,375 B1, published on March 20, 2001).

The teachings of Garvin have been summarized previously, *supra*.

Garvin does not disclose prior to lysis, treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes and increases the half-life of the RNA compared to the RNA in cells not treated with the preservation composition as recited in claim 15, wherein the salt is a sulfate salt as recited in claim 16 and the salt is ammonium sulfate as recited in claim 17, wherein the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18, wherein the salt is present in the preservation composition at a final concentration of between 20 g/100 ml and the saturating concentration of the salt as recited in claim 19, wherein the salt is present in the preservation composition at a final concentration of between 30 g/100 ml and 80 g/100 ml as recited in claim 20, wherein the RNA preservation composition comprises at least two salts as recited in claim 21 and the total salt concentration is present in the preservation composition at a final concentration of between 20 g/100 ml and 100 g/100 ml as recited in claim 22, and further comprising extracting RNA from the fractionated leukocytes with an organic extraction as recited in claim 23.

Regarding claims 15-17 and 28, since Lader teaches to use an RNA preservation medium comprising ammonium sulfate in order to protect the RNA from nucleases (see column 3, fourth paragraph), Lader discloses an RNA preservation composition (ie., ammonium sulfate) comprising a salt that infiltrates the leukocytes and increases the half-

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life of the RNA compared to the RNA in cells not treated with the preservation composition as recited in claims 15 and 28 wherein the salt is a sulfate salt as recited in claim 16 and the salt is ammonium sulfate as recited in claim 17.

Regarding claims 18-22, Lader teaches that the final salt concentration in the preservation composition is between 10 g/100 ml and a saturating concentration as recited in claim 18, the salt is present in the preservation composition at a final concentration of between 20 g/100 ml and the saturating concentration of the salt as recited in claim 19, the salt is present in the preservation composition at a final concentration of between 30 g/100 ml and 80 g/100 ml as recited in claim 20, the RNA preservation composition comprises at least two salts as recited in claim 21 and the total salt concentration is present in the preservation composition at a final concentration of between 20 g/100 ml and 100 g/100 ml as recited in claim 22 (see column 3-5).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the methods recited in claims 15-17 and 23 by treating the fractionated eukocytes with an RNA preservation composition comprising ammonium sulfate prior to lysis and contacting the RNA preservation with the matrix in view of the prior art of Garvin and Lader. One having ordinary skill in the art would have been motivated to do so because Lader teaches to use an RNA preservation medium comprising ammonium sulfate in order to protect the RNA from nucleases (see column 3, fourth paragraph) so that the half-life of the RNA is increased. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the methods recited in claims 15-17 by treating the fractionated eukocytes with an RNA preservation composition

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comprising ammonium sulfate prior to lysis and contacting the RNA preservation with the matrix in order to increase the half-life of the RNA.

10. Claims 24, 25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin in view of Korfhage *et al.*, as applied to claims 1-4, 7, 8, 10, 11, 14-18, 23, 28, and 29 above or over Garvin in view of Lader as applied to claims 1-4, 7, 8, 10, 11, 14-23, 28, and 29 above, and further in view of Maniatis *et al.*.

The teachings of Garvin and Korfhage *et al.*, or Lader have been summarized previously, *supra*.

Garvin and Korfhage *et al.*, or Lader do not disclose extracting the lysate with an organic solution to form organic and aqueous phases and separating the organic and aqueous phases as recited in claims 24 and 27. However, since Garvin in view of Korfhage *et al.*, or Lader teach claims 15 and 28 (see above rejection), Garvin in view of Korfhage *et al.*, or Lader disclose that the extracted RNA has less DNA contamination than would RNA extracted from fractionated leukocytes that were not treated with the RNA preservation medium as recited in claim 25 and fractionating leukocytes from blood by capturing them with a leukocyte depletion matrix, treating the fractionated leukocytes with an RNA preservation composition comprising a salt that infiltrates the leukocytes, increasing the half-life of the RNA, lysing the fractionated leukocytes to produce a lysate and isolating RNA as recited in claim 27.

Maniatis *et al.*, teach to extract RNA via phenol/chloroform (see page 192).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in

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the art at the time the invention was made to have performed the methods recited in claims 24 and 27 by extracting the RNA via phenol/chloroform in view of the prior art of Garvin, Korfhage *et al.*, or Lader and Maniatis *et al.*. One having ordinary skill in the art would have been motivated to do so because Garvin suggests to isolate RNA using a known manner (see page 1, [0017] and RNA isolation method taught by Maniatis *et al.*, is well known method for isolating RNA. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claims 24 and 27 using RNA isolation method taught by Maniatis *et al.*.

11. Claims 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garvin as applied to claims 1-4, 7, 8, 10, 11, 14, and 29 above, and further in view of Warrington *et al.*, (US Patent No. 7,108,969 B1, filed on September 10, 2001).

The teachings of Garvin have been summarized previously, *supra*.

Garvin does not disclose further comprising assaying for the presence or quantity of one or more RNAs in the lysate as recited in claim 30 wherein assaying comprises a Northern blot, RNase protection assay, hybridization reaction, microarray analysis, or reverse transcriptase-polymerase chain reaction analysis as recited in claim 31 wherein assaying comprises a reverse transcriptase-polymerase chain reaction further defined as real-time RT-PCR or endpoint RT-PCR as recited in claim 32, assaying comprises a microarray analysis as recited in claim 33 and the microarray analysis comprises the use of a cDNA array, spotted oligonucleotide array, or in-situ synthesized oligonucleotide array as recited in claim 34.

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Warrington *et al.*, teach that the quality and quantity of isolated RNA is examined by RT-PCR and the microarray analysis using spotted oligonucleotide array (see column 13, lines 57-67 and column 14).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have assayed for the presence or quantity of one or more RNAs in the lysate as recited in claim 30 wherein assaying comprises microarray analysis or reverse transcriptase-polymerase chain reaction analysis as recited in claim 31 wherein assaying comprises a reverse transcriptase-polymerase chain reaction further defined as real-time RT-PCR as recited in claim 32, assaying comprises a microarray analysis as recited in claim 33 and the microarray analysis comprises the use of a spotted oligonucleotide array as recited in claim 34 in view of the prior art of Garvin and Warrington *et al.*. One having ordinary skill in the art would have been motivated to do so because Garvin suggests that isolated RNA is used for different purposes such as population based genetic studies (see column 2, [0020]) and Warrington *et al.*, teach that the quality and quantity of isolated RNA is examined by RT-PCR and the microarray analysis using spotted oligonucleotide array (see column 13, lines 57-67 and column 14). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform RT-PCR and the microarray analysis using spotted oligonucleotide array in order to examine quality and quantity of the isolated RNA.

Conclusion

12. No claim is allowed.

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13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

January 5, 2007



FRANK LU
PRIMARY EXAMINER